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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,023	03/07/2001	Barbro Hemmendorff	10806-155	3513
24256	7590	09/09/2005	EXAMINER	
DINSMORE & SHOHL, LLP 1900 CHEMED CENTER 255 EAST FIFTH STREET CINCINNATI, OH 45202			CHUNDURU, SURYAPRABHA	
		ART UNIT	PAPER NUMBER	1637

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/743,023	HEMMENDORFF ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 22 June 2005.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 3,5-7,11-14,16-19,21 and 22 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 3,5-7,11-14,16-19,21 and 22 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

1. Applicants' response to the office action (after BPAI an affirmance in part decision) filed on June 22, 2005 has been entered.
2. Claims 1-2, 4, 8-10, 15, 20 are cancelled. Claims 3, 5-7, 11-14, 16-19, 21-22 are amended and are pending.

**Status of the Application**

3. Applicants' response to the office action is fully considered and found persuasive in part. All arguments have been fully considered and thoroughly reviewed, but are deemed persuasive in part for the reasons that follow. This action is made FINAL necessitated by amendment.

***New grounds of rejections necessitated by amendment***

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5-7, 11-14, 16-19, 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Builder et al. (USPN. 5,663,304).

Builder et al. teach a method of claims 5-7, 11-14, 16-19, 21-22, for production of recombinant peptides comprising fermenting cells (host cells) to produce recombinant peptides in the presence of metal salt (alkali metal salt) prior to peptide isolation (see col. 27, line 33-53, column 26, lines 34-67, column 27, 1-67, column 28, lines 15-33, column 6, lines 42-67, and column 7, lines 1-9). Builder also teach that (i) the use of metals facilitate disulfide oxidation of polypeptides and yield correct refolding of a misfolded polypeptide contained in host cells (see column 6, lines 42-60); metal salts include sodium chloride, potassium chloride, sodium phosphate, potassium phosphate (see column 28, lines 15-33, column 11, lines 42-54);

With regard to claims 5, and 22, Builder et al. teach that the pH of the cells prior to the addition of the metal salt is less than or equal to 7 (see col. 15, line 46-51, indicates that the pH range is 5-9 depending on the host organism (cells), which includes pH less than or equal to 7);

With regard to claims 12, 21, Builder et al. teach that the method includes human growth hormone as a preferred mammalian polypeptide (see column 9, lines 11-18).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, to modify or substitute the method of producing a recombinant polypeptide as taught by Builder et al. with the step of producing a recombinant human growth hormone to achieve expected advantage of developing a method for manufacturing human growth hormone. An ordinary skill in the art would have reasonable expectation of success that the method would work as suggested by Builder et al. because Builder et al. have explicitly indicated that human growth hormone is a particularly preferred mammalian polypeptide

according to their method (col. 9, line 11-20). Therefore an ordinary practitioner would have been motivated to modify the method of Builder et al. with the inclusion of the step of producing human growth hormone for the purpose of developing a method for production of human growth hormone, such modification of the method is considered functionally equivalent to the claimed method in the absence of secondary considerations.

***Response to arguments:***

5. With regard to the rejection made in the previous office action, under 35 USC 112, second paragraph, Applicants' arguments and the amendment are fully considered and the rejection is withdrawn in view of the amendment.

6. With regard to the rejection made in the previous office action under 35 USC 103(a), Applicants' arguments are fully considered and found unpersuasive. Applicants argue that the instant invention does not involve a method of refolding proteins using special buffer as taught by Builder et al. but, the instant invention is drawn to the method for the production of recombinant peptides with low amounts of trisulfides and Builder et al. does not teach this limitation. Applicants' arguments are fully considered and found unpersuasive, because

As MPEP 2111.02 notes, "If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction." This limitation in the preamble of the claim is not given patentable weight. In addition the method steps recite the production of recombinant peptides by adding metal salt during or after fermentation step, which is clearly taught by Builder et al. The

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disclosure of Builder et al. also teaches adding the metal salt after fermentation, before isolation of the recombinant peptides as discussed in the above rejection.

Applicants' particular arguments that Builder et al. teach formation of disulfide and trisulfides and teaches away the instant invention and Builder et al. reference cannot serve to create a prima-facie case of obviousness. Applicants' arguments are fully considered and found not persuasive because as stated in MPEP 2145, "A prior art reference that "teaches away" from the claimed invention is a significant factor to be considered in determining obviousness; however, "the nature of the teaching is highly relevant and must be weighed in substance. A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994), a teaching away, is a significant factor to be considered as "teaching in". In the instant case, the addition of metal salt to the method inherently facilitates the formation of disulfide or trisulfides, which is dependent on the concentration of metal salt used in the process. The instant claims do not recite any concentration of metal salt to be added, which reduces the amount of trisulfides, Further Builder et al. teach the method to produce recombinant peptides, which are correctly folded (see col. 12, line 35-54, which indicates metal salts facilitate the correct folding of recombinant polypeptides by lowering trisulfide formation). Hence the method as disclosed in the prior art of the record inherently teaches the low amounts of trisulfides and use of metal salts in producing correctly folded recombinant polypeptides, which clearly indicates the low trisulfides facilitate refolding of proteins. Further, the claim is of the open "comprising" format, which permits the inclusion of additional elements, so that any additional steps are permitted in the claim.

Applicants' further argue that Builder et al. teach pH of 3.5 after adding metal salt and the instant amended claims recite pH of the cells prior to the addition of metal salt. To address this issue the rejection is rewritten to discuss the limitations.

Applicants further argue that to establish *prima facie* obviousness one must provide enabling disclosure and argue that no teaching or suggestion is provided by Builder et al. to arrive at the instant claimed invention. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, specific motivation is provided in the rejection above, which notes that an ordinary skill in the art would have reasonable expectation of success that the method would work as suggested by Builder et al. because Builder et al. have explicitly indicated that human growth hormone is a particularly preferred mammalian polypeptide according to their method (col. 9, line 11-20). Therefore an ordinary practitioner would have been motivated to modify the method of Builder et al. with the inclusion of the step of producing human growth hormone for the purpose of developing a method for production of human growth hormone, such modification of the method is considered functionally equivalent to the claimed method in the absence of secondary considerations.

Therefore the rejection is maintained and rewritten to include the amended claims herein, as discussed above.

***Conclusion***

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

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Suryaprabha Chunduru  
Examiner  
Art Unit 1637

JEFFREY FREDMAN  
PRIMARY EXAMINER

9/1/05

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